

WHAT IS CLAIMED IS:

1. An isolated DNA comprising nucleic acid of SEQ ID NO:1 comprising an alteration wherein said alteration is selected from the group consisting of T at position 1714, G at position 1762, T at position 1841, C at position 1955, and all mutations listed in Table 7.
2. A nucleic acid probe which hybridizes to the isolated DNA of claim 1 under conditions at which it will not hybridize to a nucleic acid of SEQ ID NO:1.
3. A method for diagnosing a mutation which causes long QT syndrome comprising hybridizing a probe of claim 2 to a patient's sample of DNA or RNA, the presence of a hybridization signal being indicative of long QT syndrome.
4. A method according to claim 3 wherein the patient's DNA or RNA has been amplified and said amplified DNA or RNA is hybridized with a probe of claim 2.
5. A method according to claim 3 wherein said hybridization is performed *in situ*.
6. A method according to claim 3 wherein said assay is performed using nucleic acid microchip technology.
7. A method for diagnosing a mutation which causes long QT syndrome comprising using a single-stranded conformation polymorphism technique to assay for said mutation wherein said method uses a primer pair selected from the group consisting of:
  - 1) SEQ ID NOs:56 and 57;
  - 2) SEQ ID NOs:58 and 59;
  - 3) SEQ ID NOs:60 and 61;
  - 4) SEQ ID NOs:62 and 63;
  - 5) SEQ ID NOs:64 and 65;
  - 6) SEQ ID NOs:66 and 67;
  - 7) SEQ ID NOs:68 and 69;

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- 8) SEQ ID NOs:70 and 71;  
9) SEQ ID NOs:72 and 73;  
10) SEQ ID NOs:74 and 75;  
11) SEQ ID NOs:76 and 77;  
12) SEQ ID NOs:78 and 79;  
13) SEQ ID NOs:80 and 81;  
14) SEQ ID NOs:82 and 83;  
15) SEQ ID NOs:84 and 85;  
16) SEQ ID NOs:86 and 87;  
17) SEQ ID NOs:88 and 89;  
18) SEQ ID NOs:90 and 91;  
19) SEQ ID NOs:92 and 93; and  
20) SEQ ID NOs:94 and 95.

8. A method for diagnosing a mutation which causes long QT syndrome comprising amplifying a region of the HERG gene or RNA and sequencing the amplified gene or RNA wherein long QT syndrome is indicated by any one or more mutations of the following group: a T at base 1714 of SEQ ID NO:1, a G at base 1762 of SEQ ID NO:1, a T at 1841 of SEQ ID NO:1, a C at base 1889 of SEQ ID NO:1, and a mutation shown in Table 7.
9. A method for diagnosing a mutation which causes long QT syndrome comprising identifying a mismatch between a patient's DNA or RNA and a wild-type DNA or RNA probe wherein said probe hybridizes to a region of DNA or RNA wherein said region is any one of the following group: a region comprising base 1714 of SEQ ID NO:1, base 1762 of SEQ ID NO:1, base 1841 of SEQ ID NO:1, base 1889 of SEQ ID NO:1, and mutations shown in Table 7.
10. The method of claim 9 wherein the mismatch is identified by an RNase assay.

11. An antibody which binds to a mutant HERG polypeptide but not to wild-type HERG polypeptide, wherein said mutant polypeptide causes long QT syndrome and wherein said mutant polypeptide is a polypeptide of SEQ ID NO:2 wherein said polypeptide has a mutation selected from the group consisting of a cysteine at amino acid residue 572, an aspartic acid at amino acid residue 588, a valine at amino acid residue 614, an alanine at amino acid residue 630, and mutations shown in Table 7.
12. An antibody according to claim 11 wherein said antibody is a monoclonal antibody.
13. A method for diagnosing long QT syndrome said method consisting of an assay for the presence of mutant HERG polypeptide in a patient by reacting a patient's sample with an antibody of claim 11, the presence of a positive reaction being indicative of long QT syndrome.
14. The method of claim 13 wherein said antibody is a monoclonal antibody.
15. The method of claim 13 wherein said assay comprises immunoblotting.
16. The method of claim 13 wherein said assay comprises an immunocytochemical technique.
17. An isolated HERG polypeptide comprising a mutation which causes long QT syndrome wherein said mutation is a cysteine at amino acid residue 572, an aspartic acid at amino acid residue 588, a valine at amino acid residue 614, an alanine at amino acid residue 630, or a mutation shown in Table 7.
18. A method for diagnosing long QT syndrome, said method comprising a HERG polypeptide, a mutation in said polypeptide being indicative of long QT syndrome wherein said mutation is selected from the group consisting of a cysteine at amino acid residue 572, an aspartic acid at amino acid residue 588, a valine at amino acid residue 614, an alanine at amino acid residue 630, and mutations shown in Table 7.

19. A pair of nucleic acids selected from the group consisting of:

- 1) SEQ ID NOs:56 and 57;
- 2) SEQ ID NOs:58 and 59;
- 3) SEQ ID NOs:60 and 61;
- 4) SEQ ID NOs:62 and 63;
- 5) SEQ ID NOs:64 and 65;
- 6) SEQ ID NOs:66 and 67;
- 7) SEQ ID NOs:68 and 69;
- 8) SEQ ID NOs:70 and 71;
- 9) SEQ ID NOs:72 and 73;
- 10) SEQ ID NOs:74 and 75;
- 11) SEQ ID NOs:76 and 77;
- 12) SEQ ID NOs:78 and 79;
- 13) SEQ ID NOs:80 and 81;
- 14) SEQ ID NOs:82 and 83;
- 15) SEQ ID NOs:84 and 85;
- 16) SEQ ID NOs:86 and 87;
- 17) SEQ ID NOs:88 and 89;
- 18) SEQ ID NOs:90 and 91;
- 19) SEQ ID NOs:92 and 93; and
- 20) SEQ ID NOs:94 and 95.

20. A method of amplifying an exon of *HERG* wherein said method comprises using a pair of primers selected from the primer pairs of claim 19.

21. An isolated nucleic acid comprising SEQ ID NO:3.

22. A method to screen for drugs which are useful in treating a person with a mutation in *HERG*, wherein said mutation is one which results in a cysteine at amino acid residue 572, an aspartic acid at amino acid residue 588, a valine at amino acid residue 614, an alanine at amino acid residue 630, or a mutation shown in Table 7, said method comprising:
- a) placing a first set of cells expressing *HERG* with a mutation, wherein said mutation is a cysteine at amino acid residue 572, an aspartic acid at amino acid residue 588, a valine at amino acid residue 614, an alanine at amino acid residue 630, or a mutation shown in Table 7, into a bathing solution to measure a first induced  $K^+$  current;
  - b) measuring said first induced  $K^+$  current;
  - c) placing a second set of cells expressing wild-type *HERG* into a bathing solution to measure a second induced  $K^+$  current;
  - d) measuring said second induced  $K^+$  current;
  - e) adding a drug to the bathing solution of step (a);
  - f) measuring a third induced  $K^+$  current of cells in step (e); and
  - g) determining whether the third induced  $K^+$  current is more similar to the second induced  $K^+$  current than is the first induced  $K^+$  current, wherein drugs resulting in a third induced  $K^+$  current which is closer to the second induced  $K^+$  current than is the first induced  $K^+$  current are useful in treating said persons.
23. The method of claim 22 wherein cells of said first set of cells are transfected with a mutant *HERG* wherein said mutant *HERG* encodes a *HERG* protein with a cysteine at amino acid residue 572, an aspartic acid at amino acid residue 588, a valine at amino acid residue 614, an alanine at amino acid residue 630, or a mutation shown in Table 7.
24. The method of claim 22 wherein cells of said second set of cells are transfected with nucleic acid encoding wild-type *HERG*.
25. The method of claim 22 wherein said first set of cells or said second set of cells is obtained from a transgenic animal

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26. A vector comprising the isolated DNA of claim 1.
27. A cell transfected with the vector of claim 26.
28. A cell transfected with the DNA of claim 1.
29. A nonhuman, transgenic animal comprising the DNA of claim 1.
30. A nonhuman, transgenic animal comprising the vector of claim 26.
- (Handwritten marks: a large 'X' over claims 26-28, a circled 'B' over claim 30, and a line connecting claim 29 to claim 30.)*

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